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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,333	BIHOREAU ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57* is/are pending in the application.

4a) Of the above claim(s) *1-27 and 33-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 28 and 30 have been amended.

2. Claims 1-27 and 33-57 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 2, 2008

3. Claims 28-32 are under examination.

4. The following office action contains NEW GROUNDS of Rejection.

Oath/Declaration

5. The objection to the oath or declaration for being in a foreign language is withdrawn in view of applicant's filing a supplemental declaration.

6. The supplemental oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Objections Withdrawn

7. The objection to the specification is withdrawn in view of applicant's amendment to the specification.

8. The objection to claim 28 is withdrawn in view of applicant's amendment to the claim.

Rejections Withdrawn

9. The rejection of claims 28-32 under 35 U.S.C. 102(b) as being anticipated by Shinkawa, et al. is withdrawn in view of applicant's amendment to the claims.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claim 28 is rejected under 35 U.S.C. 102(b) as being anticipated by Shields, et al. (Journal of Biological Chemistry, 2002. Vol. 277, pages 26733-26740, as cited on the IDS filed October 30, 2008).

The claim recites therapeutic antibodies having high effector activity obtained from the method comprising: a) producing and purifying monoclonal antibodies obtained from different sources selected from the group consisting of cells, plants and

non-human animals, b) measuring the fucose content and the galactose content of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies, and c) selecting antibodies for which the fucose content/galactose content ratio is between 0.5 and 0.35.

Shields, et al. teach production of antibodies with reduced fucose content compared to galactose content (see table 1 and figure 1). Regarding the product by process claim, MPEP 2113 states "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process" In re Thorpe, 777 F.2d 695, 698,227 USPQ 964, 966 (Fed. Cir. 1985). Since the claim requires an antibody with a reduced fucose content relative to galactose and Shields, et al. teach production of an antibody in a fucosyltransferase deficient cell line resulting in an antibody with reduced fucose content relative to galactose content, the claim is anticipated by Shields, et al.

Therefore, it is the Examiner's position that Shields, et al. have produced antibodies that have the same fucose/galactose content ratio as the instantly claimed antibodies. One of ordinary skill in the art would reasonably conclude that Shields' antibody also possesses the same structural and functional properties as those of the antibodies claimed and, therefore, it appears that Shields have produced antibodies that are identical to the claimed antibody. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed antibody with the antibody

of Shields, the burden of proof is upon the Applicants to show an unobvious distinction between the structural and functional characteristics of the claimed antibody and the antibody of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shields, et al. (Journal of Biological Chemistry, 2002. Vol. 277, pages 26733-26740, as cited on the IDS filed October 30, 2008) in view of Shinkawa, et al. (Journal of Biological Chemistry, 2003. Vol. 278 pages 3466-3473, as cited on the IDS filed October 30, 2008) as evidenced by Cartron, et al. (Blood, 2002. Vol. 99, pages 754-758, as cited on the PTO-892 mailed December 8, 2008).

Claim 28 has been described supra. Claims 29-32 recite a pharmaceutical composition comprising an antibody according to claim 28 and at least one excipient, wherein the antibody is directed against a non-ubiquitous normal antigen, or an antigen of a pathological cell or on a pathogenic organism for humans, wherein said antibodies are IgGs. A pharmaceutical composition comprising at least 50% of a monoclonal antibody for which the glycanic structures borne by the glycosylation site of the Fc region have a fucose content/galactose content ratio between 0.5 and 0.35.

Shields, et al. has been described supra. Shields, et al. do not teach a pharmaceutical composition comprising the antibody and an excipient. This deficiency is made up for in the teachings of Shinkawa, et al. and Cartron, et al.

Shinkawa, et al. teach KM3065 antibodies which have higher antibody dependent cellular cytotoxicity (ADCC) (e.g., "high effector activity") than the parent Rituxan TM antibody (page 468 column 2 and figure lb). Shinkawa, et al. also teach the KM3065 antibody is an IgG1 antibody that binds to CD20, a non-Hodgkin's lymphoma

antigen (page 3468, 2nd column) Shinkawa, et al. teach the purified antibodies were placed in a buffer composition comprising sodium chloride, sodium citrate dihydrate, and polysorbate 80 which is the same buffer as that for Rituxan TM (page 3467, 1st column). Cartron, et al. teach a humanized anti-CD20 monoclonal antibody (Rituxan TM) administered in a pharmaceutical composition for the treatment of non-Hodgkin's lymphoma (page 755 1st column). Thus, buffer composition of Shinkawa, et al. comprises a pharmaceutical carrier or excipient as evidenced by Cartron, et al.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody with a reduced fucose/galactose content of Shields, et al. in a pharmaceutical composition comprising a pharmaceutical carrier or excipient as taught by Shinkawa, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an antibody with a reduced fucose/galactose content of Shields, et al. in a pharmaceutical composition as taught by Shinkawa, et al. because Shinkawa, et al. teach a similar antibody with reduced fucose content in a pharmaceutical composition. Further, Shinkawa, et al. teach the therapeutic antibodies with increased ADCC would result in the improvement of clinical response (page 3473). Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody with a reduced fucose/galactose content of Shields, et al. in a pharmaceutical composition in view of Shinkawa, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Conclusion

16. No claims are allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
September 8, 2009

/Anne M Gussow/
Examiner, Art Unit 1643

/David J Blanchard/
Primary Examiner, Art Unit 1643